

86 nitrogen atom which is optionally alkylated or a heterocyclic ring including one or more double bonds], R₅ is H, fluoro, chloro, bromo, iodo, trifluoromethyl, methyl, methoxy or phenyl and R₆ is fluoro or methyl.

Claim 78, second line below the structural formula, delete "and phenyl".

REMARKS

The above set forth amendments present claims which are believed to be prima facie allowable in the light of the Official Action of October 2, 1986. A correction has been made in Examples 10u and 11g and this change is supported by the attached declarations of James Edward Jeffrey and Gerald Haran. Since the compounds in fact prepared according to the descriptive material have an R₁ substituent as 3-butenyl, the correction has been made based on the supporting data set forth in those declarations and it is believed that this change does not involve new matter as the R₁ substituent was from the beginning 3-butenyl.

The Examiner has put forward two grounds of rejection in the Official Action. One ground is for double patenting over claims 1-29 of U.S. Patent No. 4,522,828. With respect to that rejection, Applicants submit herewith a declaration from William Roger Buckett which will be discussed in detail below. The second ground of rejection is a provisional double patenting obviousness rejection based on co-pending application serial number 725,129 in view of U.S. Patent No. 4,522,828. Applicants submit herewith a Terminal Disclaimer with respect to U.S. Patent

No. 4,522,828 and wishes to advise the Examiner that a similar Terminal Disclaimer is being submitted in serial number 725,129. Therefore, it is submitted that the double patenting obviousness rejection, should it come to fruition based on the issuance of serial number 725,129, would be obviated in view of the two terminal disclaimers filed in the respective cases.

The subject matter deleted from the claims in the present case will be covered by a separate continuation application.

Turning now to Dr. Buckett's declaration, Dr. Buckett's background and familiarity with the subject matter of the present application and the '828 patent will be found in paragraphs 1 and 2. Dr. Buckett states that he is familiar with test procedures at the Boots Company to determine therapeutic activity of compounds described and claimed in U.S. Patent No. 4,443,449 and the above application. He goes on to describe test procedures conducted on compounds set forth in the tables which were described and claimed in U.S. Patent No. 4,443,449 and are represented by formula A and compounds which are described and claimed in serial numbers 725,129, 725,206 and 812,730 which are represented by formula B. Table IA gives the RR_{30} values for the compounds identified in the examples of U.S. Patent No. 4,443,449 and Table IB gives the RR_{30} values for other compounds of formula A falling within the scope of the claims of that patent which have been prepared in the laboratories of the assignees of the present invention. This data is submitted pursuant to

Applicants' obligation for a full disclosure to the Patent Office of all test data which a reasonable Examiner could consider to be relevant to the patentability of the claims of the instant application.

In Tables II and III are the RR_{30} values for compounds of the formula A in which Ar is 4-chlorophenyl and 3,4-dichlorophenyl, respectively. In addition, those tables also include RR_{30} data on compounds of formula B in which Ar is 4-chlorophenyl and 3,4-dichlorophenyl, respectively, which are described and claimed in U.S. serial numbers 725,129, 725,206 and 812,730 and which Applicants believe are the compounds closest structurally to the compounds of the formula A.

It is Dr. Buckett's opinion that table II in which Ar in the formulae A and B is 4-chlorophenyl shows that in compounds falling within the claims of U.S. Patent No. 4,443,449 the activity decreases as the size of the group R_7 increases from methyl and ethyl to propyl whereas in the compounds of formula B falling within the claims of U.S. Serial Nos. 725,129, 725,206 and 812,730 the activity is maintained as the size of the corresponding group R_1 increases from methyl and ethyl to alkyl groups containing 3 and 4 carbon atoms. In Dr. Buckett's opinion this result could not have been predicted from the results obtained with the compounds of U.S. Patent No. 4,443,449.

In Dr. Buckett's opinion, table III shows a similar situation for compounds of formula A wherein increasing the size of the group R_7 to isobutyl results in a decrease in activity

whereas a high level of activity is maintained as the size of the group R_1 in compounds of formula B is increased. The results shown could not have been predicted from the results of the compounds of U.S. Patent No. 4,443,449.

The RR_{30} values obtained for compounds identified in the examples of U.S. Serial No. 725,206 falling within the scope of the claims are set forth in table IV. It is Dr. Buckett's opinion that table IV shows that the compounds of serial number 725,206 show superior activity to the structurally closest compounds of U.S. Patent No. 4,443,449 which are the compounds of formula A in which R_7 is propyl. The compounds in table IV also show superior activity to the compound formula A in table III in which R_7 is isobutyl.

Based on the data set forth in tables II - IV it is Dr. Buckett's opinion that the anti-depressant activity of compounds of U.S. serial number 725,206 which have the formula B as set forth in these tables could not have been predicted from the results obtained with compounds of U.S. Patent No. 4,443,449 of formula A in the tables. It is further his opinion that compounds of formula B of U.S. serial number 725,206 and table IV show unexpected superiority over compounds of U.S. Patent No. 4,443,449.

Lastly, Dr. Buckett states that table V sets forth the RR_{30} results obtained for compounds of formula B falling within the scope of the claims of the present application which have been prepared in the laboratories of the assignee of the

application and which are not included in tables II - IV. This is merely for the purpose of completing the submission of all data which a reasonable Examiner could consider relevant to the patentability of the claims of the instant application.

In the light of the foregoing, it is submitted that upon consideration of the instant declaration and recordation of the submitted terminal disclaimer the instant application is in formal condition for allowance and such action is respectfully requested at this time.

A check in the sum of \$56.00 is attached to cover the terminal disclaimer recordation fee. The Commissioner is hereby authorized to charge any deficiency in any fee associated with

this communication only to our Deposit Account No. 10-0125.

Respectfully submitted,

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April 1, 1987